

ASSOCIATION OF PLASMA CHOLINE AND BETAINE WITH ARSENIC METHYLATION

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Background and Aims: Roughly 140 million people worldwide are exposed to arsenic (As)-contaminated drinking water at concentrations exceeding the WHO standard of 10 µg/L. Metabolism of inorganic As (InAs), which facilitates urinary excretion, involves two methylation steps; both utilize S-adenosylmethionine (SAM) as the methyl donor. SAM biosynthesis relies on B vitamins including folate, but other nutrients, including choline and betaine, also contribute to the methyl pool. Folate and betaine are interdependent; they are the two complementary methyl donors used in the remethylation of homocysteine to methionine, a crucial step in SAM production. Betaine is obtained from the diet or produced endogenously from choline oxidation. The aim of this study was to investigate the associations of plasma choline and betaine with the methylation of As and to determine whether these associations differed by folate status.

Methods: We conducted a cross-sectional study of 378 Bangladeshi adults between the ages of 23 and 60 who were exposed to a wide range of As concentrations in drinking water. Plasma choline and betaine were measured using liquid chromatography tandem mass spectrometry (LC-MS/MS). Total As and As metabolites were measured in urine and blood.

Results: There were no statistically significant associations between plasma betaine or choline and urinary As metabolites among the folate-sufficient participants (n=266). Among the folate-deficient (n=112), plasma betaine and choline were inversely associated with the proportions of total urinary As excreted as InAs (betaine: $\bullet = -0.16$, $p=0.05$, choline: $\bullet = -0.02$, $p=0.0004$) and monomethylarsonic acid (betaine: $\bullet = -3.11$, $p=0.03$, choline: $\bullet = -0.39$, $p=0.005$), and positively associated with the proportion excreted as dimethylarsinic acid (betaine: $\bullet = 5.75$, $p=0.01$, choline: $\bullet = 0.80$, $p=0.0004$). Similar patterns of association were observed with blood As metabolites.

Conclusions: These findings suggest that two nutrients, choline and betaine, are favorably associated with As methylation, particularly among folate-deficient individuals.